REMARKS

Upon entry of the present amendment, claims 5-13 will be pending in the present application. New claims 10-13 have been added. Support for the new claims is provided throughout the specification, e.g., in Examples 1-3. Applicants believe that no new matter is added by the amendments.

35 U.S.C. § 102 (b)

Claims 5-9 have been rejected under 35 U.S.C. 102 (b) as allegedly anticipated by Soto et al. (*Biochem. Biophys. Res. Com.* 1996; 226:672-680). Applicants respectfully disagree with the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. (*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). Applicants maintain that Soto et al. does not meet this requirement.

Claim 5 recites

> A method of identifying whether a protein is susceptible to forming amyloid, the method comprising analyzing the amino acid sequence of the protein to determine whether the protein contains a predicted discordant helix, wherein the presence of predicted discordant helix is an indication that the protein is susceptible to forming amyloid.

The Office Action states

> Soto et al., teach the use of the Chou Fasman structure prediction algorithm to determine the probability that residues 15-25 of Aβ will form a β sheet... It is well known in the art that residues 15-25 of the Aβ protein represent residues that can form either α-helices or β-sheets... Thus, the residues taught by Soto et al., meets Applicant's definition of a "discordant helix" as defined in the instant disclosure (p. 4) as an amino acid sequence that is predicted to be able to form either an α-helix or β-sheet.

Claim 5 requires the feature of determining whether a protein contains a discordant helix – i.e., "an amino acid sequence that is predicted to be able to form an α-helix and is also

predicted to be able to form a β-strand." Soto et al. does not teach this feature. The reference only uses an algorithm to determine the probability of selected residues to form β-pleated sheet. Soto et al. does not predict α-helix. Claim 5 also requires the recognition that such a sequence (i.e., a sequence that can form α-helix and β-structure) is a particular type of sequence (a discordant sequence) and that such a structure has significance – such a structure indicates that a protein containing the sequence can form amyloid. Soto et al. does not teach any method for predicting that a protein can form amyloid. Accordingly, Soto et al. does not provide all of the features of the pending claim 5. Nor do any of the other teachings of Soto et al. provide the deficiencies described above.

The Office Action states

> Soto et al., also teach that hydrophobicity facilitates monomeric interactions that thermodynamically drive Aβ peptides to convert from α-helices to β-sheets, which produce amyloid fibrils... Applicant's claims broadly encompass Aβ peptides, among others. (Office Action at page 3, last paragraph).

As discussed in Applicant's previous Response, this is not what Soto et al. teaches. Soto et al. states "[i]t seems likely that hydrophobicity facilitates monomeric interaction and that β-sheet content drives this interaction to β-sheet oligomers and amyloid fibrils. (Soto et al. at p. 673, first paragraph). In this passage, Soto et al. appears to be discussing the monomeric interaction between β-conformation monomers to make β-sheet, and makes no reference to α-helical forms. Applicants do not believe that the Office Action has correctly interpreted the teachings of Soto et al. Applicants respectfully submit that the present Office Action has merely repeated the previous rejection without providing reason for rejecting Applicant's arguments.

In addition, Applicants are unclear and request clarification as to what is meant by "Applicants claims broadly encompass Aβ peptides, among others." Claim 5 is not drawn to a peptide. The claim is drawn to a method of identifying a sequence that can form a particular structure. Notwithstanding the statements in the Office Action, Soto et al. simply does not teach a method of identifying a protein that can form amyloid by analyzing the protein for the presence of sequence that can form α-helix and β-structure.

The Office Action also states

> Soto et al., also teach a method of determining the percentage of amyloid formed per concentration of iAβ1... thus showing that the smaller peptide inhibitors are able to successfully decrease the rate of formation of β-strand structures. Soto et al., teach that the anti-β-sheet peptides and derivatives, including cyclic peptides or peptide mimetic molecules may be used to prevent and/or retard amyloidosis in vivo in Alzheimer's disease and other types of amyloid related disorders (p. 678, last paragraph to p. 679, first paragraph)

Applicants do not understand the relevance of this passage. In fact, in the paragraph preceding the cited section, Soto et al. states

> The results of this study support the concept that the formation of a β-sheet secondary structure is related to fibrillogenesis. It is likely that anti-β-sheet peptides inhibit amyloid formation by binding to monomeric Aβ peptides thereby blocking the formation of the oligomeric β-sheet conformation precursor of the fibrils.

Thus, Soto et al. may teach blocking of binding between entities that are in a β-conformation. This is not the same approach as that taught by Applicants, which relates to stabilization of a protein that contains a discordant helix in an α-helical conformation. This was discussed by Applicants in the previous Response. However, the present Office Action does not provide any reason why Applicants' explanation of the difference between Soto et al. and Applicants' claimed invention was not accepted.

It appears that the Office Action is requiring a limit on the length of discordant helices (Office action at page 3, second full paragraph). Applicants are unclear as to why a specific limit on the length is relevant and request clarification. Nor do Applicants understand why the Office Action states "The specification does not limit the manner in which a 'discordant helix,' may be identified." (Office Action at page 3, second full paragraph). Applicants assert that such methods are known in the art.

The Office Action states

> Soto et al., also teach the use of an inhibitor of Aβ fibrilllogenesis peptide (iAβi), an 11 amino acid peptide composition that prevents the adoption of β-sheets in Aβ so that the maintenance of α-helixes is favored. Quantitative evaluation of the effect of iAβ1 on *in vitro* Aβ fibrollogenesis showed that iAβ1 was not present...
>
> Soto et al., teach that the anti-β-sheet peptides and derivatives, including cyclic peptides or peptide mimetic molecules may be used to prevent and/or retard amyloidosis in vivo in Alzheimer's disease and other types of amyloid related disorders.

This aspect of the rejection is presumably directed at Claim 7, which is drawn to

> A method of decreasing the rate of formation of β-strand structures between at least two discordant helix-containing polypeptides, the method comprising contacting the discordant helix-containing polypeptides with a compound that stabilizes an α-helical form of the discordant helix.

As discussed above, nothing in Soto et al. relates to the identification of discordant helix, nor does Soto et al. suggest the stabilization of an α-helical form of a discordant helix. The peptide disclosed in Soto et al. is designed

> based on the hypothesis that amyloid formation could be inhibited by peptides homologous to Aβ and with a similar degree of hydrophobicity, but with a very low propensity to adopt a β-sheet conformation." (Soto et al. at p. 673).

There is no suggestion by Soto et al. to stabilize an α-helix conformation of a peptide, nor is there any evidence of an effect by the inhibitor peptide of Soto et al. on α-helix conformation in Soto et al. or in the present Office Action. Because of the deficiencies of Soto et al., the reference cannot anticipate claim 7 or any other pending claim.

Claim 8 is drawn to a method of treating an individual having or at risk for an amyloidosis by administering a therapeutically effective amount of a compound that stabilizes an α-helical form of a discordant helix-containing polypeptide that forms amyloid. As discussed above, nothing in Soto et al. suggests making such a compound, much less treating a subject with such a compound. Accordingly, Soto et al. does not anticipate Claim 8.

Claim 9 depends from claim 8. For the reasons discussed above, Soto et al., does not anticipate claim 8 and therefore cannot anticipate claim 9. Furthermore, Soto et al. provides no teaching related to prion disease and therefore cannot anticipate this feature of claim 9.

In view of the arguments presented above, Applicants believe that Soto et al. does not anticipate any of the pending claims and respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

CONCLUSION

In view of the arguments presented above, Applicants believe the pending application is in condition for allowance, which action is respectfully requested.

A Petition for Extension of Time is enclosed herewith. No additional fees are believed to be due. However, if such a fee is due or a credit is owed, please make them to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

Dated: December 14, 2007

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